RHÔNE-POULENC

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Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Re: (Docket No. 99D-1738)

We at Rhone-Poulenc Rorer, Inc. have reviewed the Draft Guidance for Industry regarding the CMC and Bioavailability and Bioequivalence Studies for Nasal Aerosols and Nasal Sprays for Local Action, published by The Agency in June, 1999. Having accumulated considerable experience with pharmaceutical products of this type, we would like to offer our comments for your consideration.

We believe both draft guidances are quite thorough, encompassing a wide array of tests to insure adequate product characterization and functional comparability between products. However, there is so little evidence correlating in vitro performance with clinical outcome, e.g., the in vitro performance of the device does not necessarily indicate the deposition pattern within the nasal region. Therefore, we support the view that a considerable number of both *in vivo* and *in vitro* test measures are needed to insure consistent product performance for both Nasal Sprays and Nasal Aerosols.

At the same time, we offer two additional points for your consideration as you prepare the final guidances for nasal aerosols and nasal spray products. First, the draft states products must meet all applicable compendial standards, but it is our understanding that the USP standards for container extractables are not appropriate for this class of products. The materials in the plastic

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container components and O-rings are subject to extraction into the drug product formulation as a function of both their composition and of the inactive ingredients within the formulation. We suggest that more rigorous limits be established than those published in the USP, similar to what is now required by FDA for all innovator products.

Second, while the draft guidances do include considerable characterization and comparability testing of nasal product delivery devices, we would recommend including an imaging method test procedure as an *in vivo* confirmation of proper delivery of product.

In closing, we would like to commend the Agency for the efforts extended to develop these guidelines and would ask that all of Industry's feedback be given serious consideration because of the importance of these documents.

Sincerely,

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